

(VIIA)

where X, R^{2'}, R¹, R³, R⁵, R⁶ and R⁷ are as defined in relation to formula (I), R² is a group R² as defined in relation to formula (I) or a protected form thereof, with a compound of formula

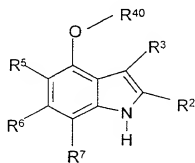
5 (VIII A)



(VIII A)

where Z, R¹⁶ and R¹⁷ are as defined above.

10 Compounds of formula (VIIA) can be prepared by reacting a compound of formula (IX)



(IX)

where R³, R⁵, R⁶ and R⁷ are as defined in relation to formula (I) and R^{2'} is as defined in
 15 relation to formula (VII) and R⁴⁰ is a protecting group; with compound of formula (X)



(X)

20 where R¹ and X are as defined in relation to formula (I) and Z¹ is a leaving group, and thereafter, removing the protecting group R⁴⁰.

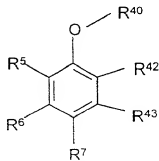
Suitable leaving groups for Z include halide such as chloride, bromide or iodide, as well as mesylate or tosylate. The reaction is suitably effected in an organic solvent such as dimethylformamide (DMF) tetrahydrofuran (THF) or DCM in the presence of a base such as sodium hydride, sodium hydroxide, potassium carbonate. Optionally the reaction is effected in the presence of a suitable phase transfer catalyst. The choice of base and solvent is interdependent to a certain extent in that certain solvents are compatible with some bases only as is understood in the art. For example, sodium hydride may preferably be used with dimethylformamide or tetrahydrofuran and sodium hydroxide is preferably used with dichloromethane and a phase transfer catalyst.

The reaction can be carried out at moderate temperatures, for example from 0 to 50°C and conveniently at about ambient temperature.

Preferably, R^{2'} is an ester group in the compound of formula IX and this may be subsequently converted to an acid or to another ester or salt, by conventional methods later in the process. For example, when X is a group SO₂ and R² is a methyl ester of carboxy, it may be converted to the corresponding carboxylic acid by reaction with lithium iodide in dry pyridine or DMF.

Suitable protecting groups R⁴⁰ include acetyl or benzyl. The reaction conditions employed will be variable depending upon the nature of the protecting group R⁴⁰ and would be apparent to a skilled person. Acetyl groups may be removed by reaction with a strong base such as sodium methoxide, whereas benzyl groups may be removed by hydrogenation for example in the presence of a catalyst such as a palladium catalyst.

Compounds of formula (IX) may be prepared by cyclisation of a compound of formula (XII)

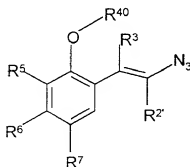


(XII)

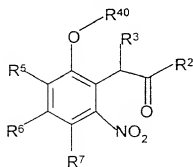
where R⁵, R⁶, R⁷ and R⁴⁰ are as defined above and R⁴² and R⁴³ represent a combination of moieties which can cyclise to form an appropriately substituted pyrrole ring. For example, one of R⁴² and R⁴³ can be a group of formula -CH=C(R⁴⁴)N₃ where R⁴⁴ is a group R² as defined above, or a protected form thereof, and the other may be hydrogen. Cyclisation to form a compound of formula (XII) may then be effected by heating for example under reflux in an organic solvent, in particular a high boiling aprotic solvent such as xylene or toluene.

Alternatively, one of R⁴² and R⁴³ may be nitro and the other may be a group of formula -CH₂C(O)R^{2'} where R^{2'} is as defined above in relation to formula (VII). These compounds will cyclise in the presence of a catalyst such as palladium on carbon in the presence of hydrogen. The reaction may be effected at moderate temperatures for example of from 0 to 80°C, conveniently at about ambient temperature.

Thus examples of compounds of formula (XII) include compounds of formula (XIII) and (XIV)



(XIII)



(XIV)

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